

**REMARKS**

Applicants herein canceled claims 29, 31-33, 36, 39-41, 43, 45, 47, 50, 52, 55-65, 71, 72, and claims 79-92. The claims are canceled for the purpose of streamlining the Examiner's consideration of two Requests for Interference filed concurrently herewith. Therefore, the claims are not canceled for any reason related to patentability and are canceled without prejudice or disclaimer. Applicants added claims 93-106. Therefore, claims 28, 30, 34, 35, 37, 38, 42, 44, 46, 48, 49, 51, 53, 54, 66-70, 73-78, and 93-106 are presently before the Examiner for consideration. Entry of the amendment is respectfully requested.

Applicants submit herewith Appendix A, which includes tables reflecting the correlation of Applicants' claims vis-a-vis U.S. Patent No.'s 6,420,114, 6,613,529, and 6,513,968. The relationship between Applicants' claims and those in the patents are briefly described below.

Applicants' claims 28, 30, 34, 37, 38, 42, 48, 49, 51, 53, and 54 are identical to claims 1, 3, 9, 13, 14, 16, 22, 23, 25, 29, and 30, respectively, of U.S. Patent No. 6,420,114 to Bedilion, issued July 16, 2002. Applicants' claims 35, 44, and 46 are directed to substantially the same invention as claims 10, 18, and 20, respectively, of U.S. Patent No. 6,420,114 to Bedilion.

Claims 66, 67, 68, 69, 70, and 73-78 are identical to claims 20, 21, 22, 24, 26, and 30-35, respectively, of U.S. Patent No. 6,513,968, issued to Schembri on February 4, 2003.

Newly added claims 93, 94, 95, 97, 98, 99, 102, 103, 104, 105, and 106, are identical to claims 1, 3, 9, 13, 14, 16, 22, 23, 25, 29, and 30, respectively, of U.S. Patent No. 6,613,529 to Bedilion, which issued on September 2, 2003.

Newly added claims 96, 100, and 101 are directed to substantially the same invention as claims 10, 18, and 20, respectively, of U.S. Patent No. 6,613,529 to Bedilion.

A table providing citations to Applicants' disclosure supporting newly added claims 93-106 can be found in the Requests for Interference submitted herewith under 37 C.F.R. §1.607.

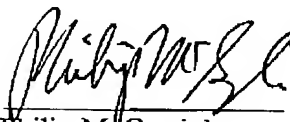
The newly added claims present no new matter.

Entry of the foregoing is respectfully requested.

No new fees are believed to be due with the filing of this document. However, the Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account 01-0431.

Respectfully submitted,  
AFFYMETRIX, INC.

Date: 1-27-04

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**APPENDIX A****Correlation Of '224 Application Claims To Bedilion And Schembri Patents**

<b>Applicants' Pending Claims</b>	<b>Bedilion 6,420,114</b>
28	1
30	3
34	9
35	10
37	13
38	14
42	16
44	18
46	20
48	22
49	23
51	25
53	29
54	30

<b>Applicants' Pending Claims</b>	<b>Schembri 6,513,968</b>
66	20
67	21
68	22
69	24
70	26
73	30
74	31
75	32
76	33
77	34
78	35

Applicants' Pending Claims	Bedilion 6,613,529
93	1
94	3
95	9
96	10
97	13
98	14
99	16
100	18
101	20
102	22
103	23
104	25
105	29
106	30

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

DONALD M. BESEMER et al

Serial No. 10/619,224

Filed: July 12, 2003

For: BIOARRAY CHIP REACTION  
APPARATUS AND ITS MANUFACTURE

\_\_\_\_\_  
COMMISSIONER OF PATENTS  
Alexandria, VA 22313

Sir:

)  
)  
) Examiner: David A. Redding  
)  
) Art Unit: 1744  
)  
) Request for Declaration of Interference  
) with a Patent under 37 CFR §1.607 -  
) Expedited Handling

REMARKS

In accordance with 37 C.F.R. §1.607, Applicants hereby request an interference with United States Patent No. 6,513,968, which issued to Schembri on February 4, 2003. To facilitate consideration of this request, Applicants attach a proposed PTO-850 "Interference Initial Memorandum" outlining the requested interference.

Applicants herein comply with the provisions of 37 C.F.R. §1.607, which require the following:

- (1) Identify the patent;
- (2) Present a proposed count;
- (3) Identify at least one claim in the patent corresponding to the proposed count;
- (4) Present at least one claim corresponding to the proposed count or identify at least one claim already pending in its application that corresponds to the proposed count, and, if any claim of the patent or application identified as corresponding to the proposed count does not correspond exactly to the proposed count, explain why each such claim corresponds to the proposed count; and
- (5) Apply the terms of any application claim,
  - (i) Identified as corresponding to the count, and

(ii) Not previously in the application to the disclosure of the application.

(6) Explain how the requirements of 35 U.S.C. § 135(b) are met, if the application claim identified as corresponding to the proposed count was not present in the application until more than one year after the issue date of the patent.

**37 C.F.R. §1.607(a)(1) – Identification of Involved Patent**

In accordance with 37 C.F.R. §1.607(a)(1), Applicants identify U.S. Patent No. 6,513,968 to Schembri ("the '968 patent").

**37 C.F.R. §1.607(a)(2) – Proposed Count**

In accordance with 37 C.F.R. §1.607(a)(2), Applicants propose a count defined as follows:

Claim 20 of the '968 patent

or

Applicants' Claim 66

The claims defining the proposed count contain identical language, which reads as follows:

A method comprising:

providing a first substrate and a second substrate having inner surfaces that

define a closed chamber therebetween, said chamber adapted to retain a quantity of fluid so that the fluid is in contact with both inner surfaces, and wherein at least one of said inner surfaces is functionalized with polynucleotides, polypeptides, or polysaccharides;

introducing a fluid containing a plurality of components into the closed chamber so as to provide a quantity of fluid therein in contact with both inner surfaces;

providing a bubble in the fluid; and

moving a bubble within the fluid to result in mixing.

**37 C.F.R. §1.607(a)(3) – Patent Claims Corresponding to the Proposed Count**

In accordance with 37 C.F.R. §1.607(a)(3), Applicants identify claims 20-26 and 30-35 of the '968 patent as corresponding to the proposed count. Claim 20 is expressly recited in the definition of the proposed count and claims 21-26 and 30-35 define the same patentable invention as the proposed count, as explained below.

Claims 1-19 of the '968 patent are not designated as corresponding to the proposed count because the claims recite an apparatus comprising a means for "nucleating bubbles". As each bubble is nucleated and dispelled in the reaction chamber, the fluid is displaced resulting in mixing of the fluid. Likewise, claims 27-29 of the '968 patent are not designated as corresponding to the proposed count because the claims recite a method comprising a step of moving the bubble using discrete sources for creating individual bubbles at selected locations within the apparatus. These claims appear to be distinguishable from the proposed count, which does not require bubble nucleation (*i.e.*, formation) within the reaction chamber.



**37 C.F.R. §1.607(a)(4) – Application Claims Corresponding to the Proposed Count**

In accordance with 37 C.F.R. §1.607(a)(4), Applicants identify Applicants' claims 66-70 and 73-78 as corresponding to the proposed count. Applicants' claim 66 is expressly recited in the definition of the proposed count and Applicants' claims 67-70 and 73-78 define the same patentable invention as the proposed count, as explained below.

**37 C.F.R. § 1.601(n) - Claims Defining The Same Patentable Invention**

37 C.F.R. § 1.601(n) provides, in part, as follows:

Invention "A" is the *same patentable invention* as an invention "B" when invention "A" is the same as (35 U.S.C. 102) or is obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A".

In the context of this request for interference, a claim (*i.e.*, "Invention A") is directed to the same patentable invention as a proposed count (*i.e.*, "Invention B") when the claim is the same or is obvious in view of the proposed count, assuming the proposed count is prior art with respect to the claim. Below, Applicants explain why the identified patent and application claims define the same patentable invention as the proposed count and, therefore, should be designated as corresponding to the proposed count.

**Claims 20-26 and 30-35 of the '968 Patent**

Claims 20-26 and 30-35 of the '968 patent define the same patentable invention as the proposed count and, therefore, should be designated as corresponding to the proposed count for at least the following reasons:

1. **Claim 20.** Claim 20 is expressly recited in the definition of the proposed count.

Therefore, claim 20 defines the same patentable invention as the proposed count.

2. **Claim 21.** Claim 21 depends from claim 20 and further recites that the polynucleotide recited in claim 20 is a polyribonucleotide. It would have been obvious to one of ordinary skill in the art to employ a substrate comprising polyribonucleotides in view of the method defined by the proposed count. The proposed count recites a substrate functionalized with polynucleotides. It was well known in the art that polynucleotides include polydeoxyribonucleotides and polyribonucleotides. Moreover, it was well known in the art to use polydeoxyribonucleotides and polyribonucleotides on solid substrates in hybridization assays. See, for example, U.S. Patent No. 5,945,334, Col. 5, lines 28-30, and WO 95/33846, page 7, lines 4-6, which teach "chips containing an array of genetic probes such as an array of diverse RNA or DNA probes."<sup>1,2</sup> See also U.S. Patent No. 5,910,288, Col. 8, lines 13-20, which contains the following disclosure:

In certain embodiments, the apparatus additionally comprises a plurality of chemical, biochemical, or biological moieties attached to at least one of the inner face of the first surface or the inner face of the second surface. Such chemical, biochemical, or biological moieties are preferably selected from the group consisting of DNA, RNA, proteins, reagents, and combinations, derivatives, and modifications thereof.<sup>3</sup>

<sup>1</sup> U.S. Patent No. 5,945,334, was filed on June 7, 1995, issued on August 31, 1999, and therefore constitutes prior art against the '968 patent under 35 U.S.C. § 102(e).

<sup>2</sup> International Patent Publication No. WO 95/33846 was filed on June 8, 1995, and published on December 14, 1995, and therefore constitutes prior art against the '968 patent under 35 U.S.C. § 102(b).

<sup>3</sup> U.S. Patent No. 5,910,288, was filed on July 10, 1997 and issued on June 8, 1999, and therefore constitutes prior art against the '968 patent under 35 U.S.C. § 102(e).

Therefore, one of ordinary skill in the art would have readily understood that polyribonucleotides are encompassed by the recitation of polynucleotides in the proposed count because polyribonucleotides were a well known type of polynucleotides in such assays.

3. **Claim 22.** Claim 22 is listed in the '968 patent as depending from claim 2.

However, based on a review of the '968 file history, it appears that the listed dependency of claim 22 may be the result of a printing error and that claim 22 may correctly depend from claim 20. (See, for example, original claims 61 and 63 in USSN 09/137,963 and corresponding claims 20 and 22 in the '968 patent.) At the same time, however, the dependency of claim 22 on claim 2 does not appear to be necessarily improper or illogical. No certificate of correction has been entered in the '968 patent file.

In view of the possibility that claim 22 should properly depend from claim 20, for the purpose of requesting the interference, Applicants herein identify claim 22 as corresponding to the proposed count and provide the requisite explanation for such designation. Once the requested interference is declared, Schembri will have ample opportunity either to request a certificate of correction to correct the dependency of claim 22 or to move to have claim 22 designated as not corresponding to the proposed count.

Claim 22 recites a film of fluid in contact with the inner surfaces of the chamber, whereas the proposed count recites a quantity of fluid in contact with the inner surfaces of the chamber. Chambers adapted to retain a film of fluid were known in the art. For example, the Abstract of U.S. Patent No. 5,910,288, discloses an invention that "relates to a method and apparatus for

mixing thin films of fluid, particularly thin films of chemical, biochemical, or biological fluids undergoing reactions." At col. 2, lines 60-64, the '288 patent discloses an apparatus for mixing a thin film of fluid undergoing a reaction, wherein the apparatus comprises first and second surfaces having inner faces defining a thin fluid chamber between the surfaces. It would have been obvious to one of ordinary skill in the art that a relatively small volume of fluid would be introduced into the closed chamber recited in the proposed count, thereby providing a "film of fluid." Accordingly, in the context of the method defined by the proposed count, any technical distinction between a "quantity of fluid" and a "film of fluid" would have been obvious to one of ordinary skill in the art and, therefore, would define the same patentable invention as the proposed count.

4. **Claims 23, 25 and 26.** Claim 23 depends from claim 22 and further recites that the chamber is up to several millimeters in thickness. Claims 25 and 26, respectively, further define the chamber as up to three millimeters in thickness and up to two millimeters in thickness.

Reaction chambers with dimensions recited in claims 23, 25 and 26 were well known in the art. See, for example, U.S. Patent No. 5,945,334, Col. 7, lines 4-5, and WO 95/33846, page 9, lines 15-17, which teach a cavity (reaction chamber) with a depth of about 0.2 inches (5.1 millimeters). U.S. Patent No. 5,945,334, at Col. 11, lines 11-14, and WO 95/33846, at page 14, lines 41-43, also teach a cavity with a depth of about 0.07 inches (1.8 millimeters). See also U.S. Patent No. 5,910,288, Col. 4, lines 45-50, which teaches a reaction chamber from about 1 micron to about 5 millimeters in thickness; from about 3 microns to about 1 millimeter in thickness; and

from about 5 microns to about 100 microns in thickness. In view of these teachings, it would have been obvious to one of ordinary skill in art that the thickness (depth) of the reaction chamber could vary in thickness from 1 micron up to several millimeters in thickness. As reflected in these references, such chambers are suited to accommodate the relatively small volumes of fluid ordinarily involved with methods involving surfaces functionalized with polynucleotides, polypeptides or polysaccharides, such as those recited in the proposed count.

5. **Claim 24.** Claim 24 depends from claim 23 and further recites that the inner surfaces of the first and second substrates are substantially parallel. The '968 patent does not define the term "substantially parallel" but the term is used in the description of Figures 1 and 3 at Col. 3, lines 17-20 and 26-29 ("wherein the first substrate 10 is substantially parallel to the second substrate 11 with a seal 15 in between"). Apparatuses comprising chambers with substantially parallel substrates were well known in the art. See, for example, U.S. Patent No. 5,945,334, and WO 95/33846, Figures 6, 18, 19, 20b, 21, and 22. Therefore, the subject matter of claim 24 would have been obvious to one of ordinary skill in the art because reaction chambers having substantially parallel substrates were known in the art and it would have been obvious to use such a chamber to retain a quantity of fluid, as recited in the proposed count.

6. **Claim 30.** Claim 30 depends from claim 20 and further recites that at least one of the inner surfaces is functionalized with polynucleotides. The proposed count expressly recites an inner surface functionalized with polynucleotides and, therefore, claim 30 defines the same patentable invention as the proposed count.

7. **Claim 31.** Claim 31 depends from claim 20 and further recites that at least one of said inner surfaces is functionalized with polypeptides. The proposed count expressly recites an inner surface functionalized with polypeptides and, therefore, claim 31 defines the same patentable invention as the proposed count.

8. **Claim 32.** Claim 32 corresponds to claim 20, except that claim 32 recites an array of DNA and RNA probes and further recites steps of removing the sample after hybridization is complete and analyzing the functionalized inner surface. As explained in the context of claim 21, one of ordinary skill in the art would have readily understood that the recitation of polynucleotides in the proposed count encompassed DNA and RNA probes. To the extent such embodiments would not have been considered inherently defined in the proposed count, they would have been immediately obvious to one of ordinary skill in the art in view of the proposed count. Moreover, it would have been obvious to one of ordinary skill in the art to remove the sample (*i.e.*, the fluid) from the apparatus after hybridization is complete thereby removing unbound targets prior to analysis and reducing background signals. *See* U.S. Patent No. 5,800,992.<sup>4</sup> Likewise, it would have been obvious to one of ordinary skill in the art to analyze the substitute to evaluate hybridization results which would be the practical purpose for conducting the method defined by the proposed count. Accordingly, the additional recitations in claim 32 would have been obvious to one of ordinary skill in the art in view of the proposed count.

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<sup>4</sup> U.S. Patent No. 5,800,992, was filed on June 25, 1996, issued on September 1, 1998, and therefore constitutes prior art against the '968 patent under 35 U.S.C. § 102(e).

9. **Claim 33.** Claim 33 depends from claim 32 and further recites heating the DNA or RNA containing sample fluid while in the closed chamber. The step of heating a sample fluid in a closed chamber was known in the art and would have been obvious to one of ordinary skill in the art in view of the proposed count. See, for example, U.S. Patent No. 5,945,334, Col. 9, line 64, to Col. 10, line 2, and WO 95/33846, page 13, lines 12-18, which teach a temperature control mechanism that transfers heat via conduction to the fluid in the cavity. One of ordinary skill in the art would have considered such heating to be obvious because DNA and RNA hybridization reactions are ordinarily conducted at elevated temperatures. Therefore, claim 33 would have been obvious in view of claim 32 and the proposed count.

10. **Claim 34.** Claim 34 depends from claim 33 and further recites washing the functionalized inner surface prior to the analyzing to eliminate background signals produced by unbound targets. It would have been obvious to one of ordinary skill in the art to wash the substrate prior to analyzing. See, for example, U.S. Patent No. 5,945,334, Col. 15, lines 44-48, and WO 95/33846, page 21, lines 3-9, which teach washing the substrate with a buffer to remove unbound targets and thereafter conducting detection steps. See also U.S. Patent No. 5,800,992.

11. **Claim 35.** Claim 35 depends from claim 32 and further recites that the bubble is moved in a circular pattern. It would have been obvious to one of ordinary skill in the art to move the bubble in a circular pattern to effectuate mixing.

In conclusion, claims 20-26 and 30-35 of the '968 patent define the same patentable invention as the proposed count and, therefore, should be designated as corresponding thereto.

**Applicants' Claims 66-70 and 73-78**

Likewise, Applicants' claims 66-70 and 73-78 define the same patentable invention as the proposed count and, therefore, should be designated as corresponding thereto for at least the following reasons:

1. Claim 66 is expressly recited in the definition of the proposed count. Therefore, claim 66 defines the same patentable invention as the proposed count.
2. Claims 67-70 and 73-78 are substantially identical to claims 21, 22, 24, 26 and 30-35, respectively, of the '968 patent and, therefore, define the same patentable invention as the proposed count for the reasons set forth above with respect to the '968 patent claims.

In conclusion, Applicants' claims 66-70 and 73-78 define the same patentable invention as the proposed count and, therefore, should be designated as corresponding thereto.

**37 C.F.R. §1.607(a)(5) – Applying Terms of Application Claims to Disclosure**

Applicants' claims 66-70 and 73-78 are already pending in the application but have not yet been substantively examined. Accordingly, Applicants apply the terms of claims 66-70 and 73-78 to the disclosure of the application in the table set forth below.

<u>'968 patent claims</u>	<u>Applicants' claims</u>	<u>Support in Applicants' present specification</u>
20. A method comprising: providing a first substrate	66. A method comprising: providing a first substrate and a second substrate having	Page 3, lines 8-14; Figures 6, 18, 19, 20B, 21, 22 and 27B; Page 12, lines 3-11;



<u>'968 patent claims</u>	<u>Applicants' claims</u>	<u>Support in Applicants' present specification</u>
and a second substrate having inner surfaces that define a closed chamber therebetween,	inner surfaces that define a closed chamber therebetween,	Page 26, line 19 to Page 27, line 5
said chamber adapted to retain a quantity of fluid so that the fluid is in contact with both inner surfaces,	said chamber adapted to retain a quantity of fluid so that the fluid is in contact with both inner surfaces,	Page 2, lines 18-22; Page 9, lines 23-25; Figure 3; Page 10, lines 17-24; Page 13, lines 9-13; Page 16, line 31 to Page 17, line 5; Figure 34; Page 17, lines 10-16; Figure 35; Page 24, lines 1-2 and 13-14; Page 25, line 22 to Page 26, line 17; Page 29, lines 10-19; Page 31, lines 5-8
and wherein at least one of said inner surfaces is functionalized with polynucleotides, polypeptides, or polysaccharides;	and wherein at least one of said inner surfaces is functionalized with polynucleotides, polypeptides, or polysaccharides;	Page 2, lines 18-21; Page 3, lines 2-6; Page 5, line 31 to Page 6, line 3; Page 6 lines 20-26; Page 7, line 29 to Page 8, line 6
introducing a fluid containing a plurality of components into the closed chamber so as to provide a quantity of fluid therein in contact with both inner surfaces;	introducing a fluid containing a plurality of components into the closed chamber so as to provide a quantity of fluid therein in contact with both inner surfaces;	Page 6, lines 4-18; Page 10, lines 17-24; Page 22, line 19 to Page 23, line 7; Page 28, lines 1-2; Page 29, lines 9-19; Page 30, lines 17-22
providing a bubble in the fluid; and moving a bubble within the fluid to result in mixing.	providing a bubble in the fluid; and moving a bubble within the fluid to result in mixing.	Page 10, lines 17-24; Page 28, lines 5-6
21. A method according to claim 20 wherein the polynucleotide is a polyribonucleotide.	67. A method according to claim 66, wherein the polynucleotide is a polyribonucleotide.	Page 6, line 2; Page 8, lines 1-2

<u>'968 patent claims</u>	<u>Applicants' claims</u>	<u>Support in Applicants' present specification</u>
22. A method according to claim 2 [ <i>sic</i> 20?], wherein the chamber is adapted to retain a film of fluid in contact with both inner surfaces.	68. A method according to claim 66, wherein the chamber is adapted to retain a film of fluid in contact with both inner surfaces.	Page 2, lines 18-22; Page 9, lines 23-25; Figure 3; Page 10, lines 17-24; Page 13, lines 9-13; Page 16, line 31 to Page 17, line 5; Figure 34; Page 17, lines 10-16; Figure 35; Page 24, lines 1-2 and 13-14; Page 25, line 22 to Page 26, line 17; Page 29, lines 10-19
24. A method according to claim 23 wherein the inner surfaces of the first and second substrates are substantially parallel.	69. A method according to claim 66 wherein the inner surfaces of the first and second substrates are substantially parallel.	Page 12, lines 3-11; Page 26, line 19 to Page 27, line 5; Figures 6, 18, 19, 20B, 21, 22 and 27B
26. A method according to claim 25 wherein the chamber is up to two millimeters in thickness.	70. A method according to claim 66, wherein the chamber is less than two millimeters in thickness.	Page 16, lines 18-19
30. The method of claim 20 wherein the at least one of said inner surfaces is functionalized with polynucleotides.	73. A method of claim 66, wherein the at least one of said inner surfaces is functionalized with polynucleotides.	Page 6, lines 2 and 20-26; Page 8, lines 1-2
31. The method of 20 wherein the at least one of said inner surfaces is functionalized with polypeptides.	74. A method of 66, wherein the at least one of said inner surfaces is functionalized with polypeptides.	Page 5, line 34 to Page 6, line 3
32. A method comprising: providing a first substrate and a second substrate having inner surfaces that define a closed chamber therebetween,	75. A method comprising: providing a first substrate and a second substrate having inner surfaces that define a closed chamber therebetween,	Page 3, lines 8-14; Figures 6, 18, 19, 20B, 21, 22 and 27B; Page 12, lines 3-11; Page 26, line 19 to Page 27, line 5

<u>'968 patent claims</u>	<u>Applicants' claims</u>	<u>Support in Applicants' present specification</u>
said chamber adapted to retain a quantity of fluid so that the fluid is in contact with both inner surfaces,	said chamber adapted to retain a quantity of fluid so that the fluid is in contact with both inner surfaces,	Page 2, lines 18-22; Page 9, lines 23-25; Figure 3; Page 10, lines 17-24; Page 13, lines 9-13; Page 16, line 31 to Page 17, line 5; Figure 34; Page 17, lines 10-16; Figure 35; Page 24, lines 1-2 and 13-14; Page 25, line 22 to Page 26, line 17 Page 29, lines 10-19
and wherein at least one of said inner surfaces is functionalized with an array of RNA or DNA probes;	and wherein at least one of said inner surfaces is functionalized with an array of RNA or DNA probes;	Page 2, lines 18-21; Page 3, lines 2-6; Page 5, line 31 to Page 6, line 3; Page 6, lines 20-26; Page 7, line 29 to Page 8, line 6
introducing a fluid sample containing DNA or RNA into the closed chamber so as to provide a quantity of fluid therein in contact with both inner surfaces;	introducing a fluid sample containing DNA or RNA into the closed chamber so as to provide a quantity of fluid therein in contact with both inner surfaces;	Page 6, lines 4-18; Page 10, lines 17-24; Page 22, line 19 to Page 23, line 7; Page 28, lines 1-2; Page 29, lines 10-19; Page 30, lines 17-22
providing a bubble in the fluid; moving a bubble within the fluid to result in mixing;	providing a bubble in the fluid;	Page 10, lines 17-24; Page 28, lines 5-6
after hybridization is complete, removing the sample from the apparatus; and	after hybridization is complete, removing the sample from the apparatus; and	Page 23, lines 5-7; Page 29, lines 17-19; Page 30, line 29 to Page 31, line 9
analyzing the functionalized inner surface for DNA or RNA that has hybridized.	analyzing the functionalized inner surface for DNA or RNA that has hybridized.	Page 23, lines 8-16

<u>'968 patent claims</u>	<u>Applicants' claims</u>	<u>Support in Applicants' present specification</u>
33. A method according to claim 32 additionally comprising heating the DNA or RNA containing sample fluid while in the closed chamber.	76. A method according to claim 75 additionally comprising heating the DNA or RNA containing sample fluid while in the closed chamber.	Page 2, lines 22-25; Page 14, line 22 to Page 15, line 3
34. A method according to claim 33 additionally comprising washing the functionalized inner surface prior to the analyzing.	77. A method according to claim 76 additionally comprising washing the functionalized inner surface prior to the analyzing.	Page 23, lines 5-7
35. A method according to claim 32 wherein the bubble is moved in a circular pattern.	78. A method according to claim 75, wherein the bubble is moved in a circular pattern.	Page 29, lines 15-16

**37 C.F.R. §1.607(a)(6) – Applicants Have Satisfied The Requirements of 35 U.S.C. §**

**135(b)**

In accordance with 37 C.F.R. §1.607(a)(6), Applicants have complied with the requirements of 35 U.S.C. §135(b).

The '968 patent issued on February 4, 2003. Applicants presented claims 66-70 and 73-78 on July 12, 2003, *i.e.*, less than one year after the issue date of the '968 patent.

The application from which the '968 patent issued (USSN 09/782,542) was published on August 2, 2001, *i.e.*, more than one year prior to the date on which Applicants presented claims 66-70 and 73-79. See U.S. Published Application No. 2001/0010661. However, the published independent claims recite a means or a step for nucleating a bubble in the fluid, which is a limitation not recited in the proposed count or any of the claims designated as corresponding thereto. During the prosecution of the parent application of the '968 patent (USSN 09/137,963,

which issued as U.S. Patent No. 6,186,659), Schembri emphasized that "nucleating" bubbles was a unique means for introducing bubbles into the reaction chamber. See Amendment A, received on February 29, 2000 (Attachment 1). Indeed, the Examiner's statement of reasons for allowance of the '659 patent claims states "instant claims 1-46 are allowable over the prior art because the prior art does not fairly teach or fairly suggest, alone or in combination, an apparatus or device that mixes by creating bubbles at selected locations and dispelling or moving the created bubbles". See Notice of Allowance dated August 20, 2000 (Attachment 2). Accordingly, the published application claims do not define the same or substantially the same invention as Applicants' claims 66-70 and 73-78 and, therefore, the published application claims do not raise a bar against Applicants' claims under 35 U.S.C. §135(b) (2).

In view of the above, Applicants have complied with the requirements of 35 U.S.C. §135(b).

#### **Benefit of Earlier Filed Application**

For the purpose of the requested interference, Applicants are entitled to the benefit of the June 8, 1994, filing date of USSN 08/255,682, which constitutes a constructive reduction to practice of an embodiment within the scope of the proposed count. As reflected in the table below, the '682 application discloses an embodiment within the scope the proposed count (*i.e.*, Applicants' claim 66)

<b><u>Proposed Count (Applicants' claim 66)</u></b>	<b><u>Support in the '682 specification</u></b>
A method comprising: providing a first substrate and a second substrate having inner surfaces that define a closed chamber therebetween,	Page 13, lines 7-19; Page 24, line 30 to Page 25, line 19; Figures 6, 18, 19, 20B, 21, 22, and 27B
said chamber adapted to retain a quantity of fluid so that the fluid is in contact with both inner surfaces,	Page 2, lines 21-28; Page 10, lines 14-16; Figure 3; Page 11, lines 11-22; Page 14, lines 21-28; Page 21, lines 21-23; Page 22, lines 2-4; Page 23, line 26 to Page 24, line 26; Page 28, lines 3-16; Page 30, lines 11-16

and wherein at least one of said inner surfaces is functionalized with polynucleotides, polypeptides, or polysaccharides;	Page 2, lines 21-28; Page 3, lines 3-10; Page 5, lines 23-33; Page 6, lines 23-33; Page 8, lines 7-19
introducing a fluid containing a plurality of components into the closed chamber so as to provide a quantity of fluid therein in contact with both inner surfaces;	Page 6, line 36 to Page 7, line 18; Page 11, lines 11-22; Page 19, line 31 to Page 20, line 22; Page 26, lines 20-22; Page 28, lines 1-16; Page 29, lines 21-28.
providing a bubble in the fluid; and moving a bubble within the fluid to result in mixing.	Page 11, lines 11-22; Page 26, lines 26-27

**37 C.F.R. §§ 1.601(m) and 1.608(b)**

37 C.F.R. § 1.601(m) provides that a senior party in an interference is the party with the earliest effective filing date as to the count.

As noted, Applicants' present disclosure is entitled to the benefit of a filing date of June 8, 1994, *i.e.*, the filing date of USSN 08/255,682. In comparison, the earliest possible effective filing date to which the '968 patent could be accorded benefit appears to be August 21, 1998, *i.e.*, the filing date of USSN 09/137,963. Therefore, Applicants have an effective filing date over 4 years prior to the earliest possible effective filing date of the '968 patent.

In accordance with the provisions of 37 C.F.R. § 1.601(m), Applicants should be designated the Senior Party in the requested interference.

In view of Applicants' earlier effective filing date with respect to the '968 patent, no showing under 37 C.F.R. §1.608(b) is required.

**37 C.F.R. §1.607(b) - Request to Proceed with Special Dispatch**

In accordance with 37 C.F.R. §1.607(b), Applicants request that the Examiner proceed with special dispatch in declaring the requested interference.

Respectfully submitted,  
AFFYMETRIX, INC.

Date: 1-28-04

By: Philip McGarrigle  
Philip McGarrigle  
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CERTIFICATE OF MAILING  
I hereby certify that this paper is being deposited with the U.S. Postal Service as first class mail in an envelope addressed to:  
Assistant Commissioner of Patents Washington, D.C. 20231, on the date listed below.

*Elizabeth Miller*  
Elizabeth Miller

FEB 29 2000

2/24/00  
Date

ATTY DOCKET NO. 10971849-1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Carol T. Schembri Group Art Unit: 1744  
Serial No.: 09/137,963 Examiner: Leigh McKane  
Filed: 08/21/98  
Title: APPARATUS AND METHOD FOR MIXING A FILM OF FLUID

Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

AMENDMENT AND RESPONSE

Please make the amendments to the claims indicated below. For the convenience of the Examiner all of the pending claims are reproduced below although only those indicated (claims 16 and 18) are being amended:

Sub  
P1  
1. An apparatus for mixing a film of fluid, comprising:  
a first substrate and a substantially parallel second substrate having inner surfaces that define a closed chamber therebetween, said chamber adapted to retain a quantity of fluid so that the fluid is in contact with both inner surfaces; and means for nucleating bubbles in the fluid comprising discrete heat sources for creating individual bubbles at selected locations within the apparatus, whereby, as each bubble is nucleated and dispelled, the fluid is displaced resulting in mixing.

2. The apparatus of claim 1, further comprising means for moving a bubble in the fluid.

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ATTACHMENT 1

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3. The apparatus of claim 1 wherein said means for nucleating bubbles also comprises means for moving a bubble in the fluid.
4. The apparatus of claim 1 wherein the closed chamber has a thickness of less than about 1 millimeter.
5. The apparatus of claim 4 wherein the closed chamber has a thickness of less than about 100 microns.
6. The apparatus of claim 1 wherein one of said inner surfaces is functionalized with reactive moieties.
7. The apparatus of claim 1 wherein each of said inner surfaces is functionalized with reactive moieties.
8. The apparatus of claim 6 wherein the reactive moieties comprise monomeric species covalently bound to said inner surface, each of the monomeric species having at least one reactive site.
9. The apparatus of claim 8 wherein the monomeric species are nucleotides.
10. The apparatus of claim 8 wherein the monomeric species are amino acids.
11. The apparatus of claim 6 wherein the reactive moieties comprise reactive sites of monomeric species present at the terminus of a surface-bound polymer.
12. The apparatus of claim 11 wherein the surface-bound polymer comprises a polynucleotide.

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13. The apparatus of claim 11 wherein the surface-bound polymer comprises a polyribonucleotide.

14. The apparatus of claim 11 wherein the surface-bound polymer comprises a polypeptide.

15. The apparatus of claim 1, wherein the means for nucleating bubbles comprises a discrete heat source adjacent one of said inner surfaces.

<sup>20</sup>  
16. (AMENDED) The apparatus of claim 1 wherein the means for nucleating bubbles comprises [a] discrete heat [source] sources adjacent said inner surfaces.

<sup>20</sup>  
17. The apparatus of claim 1 wherein the means for nucleating bubbles comprises a discrete heat source adjacent each said inner surface.

<sup>21</sup> <sup>20</sup>  
18. (AMENDED) The apparatus of claim 16 wherein the discrete heat [source is a resistor] sources are resistors.

19. The apparatus of claim 16 wherein the means for nucleating bubbles comprises a plurality of discrete heat sources adjacent said inner surface.

20. The apparatus of claim 18 wherein the discrete heat sources comprise resistors arranged in a predetermined pattern.

21. The apparatus of claim 1, further including a seal between the inner surface of the first substrate and the inner surface of the second substrate.

22. The apparatus of claim 21 wherein the seal is flexible.

23. The apparatus of claim 1, further including a means for introducing fluid into the closed chamber to provide a film of fluid therein.

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24. The apparatus of claim 1 wherein each of the first substrate and the second substrate individually comprises a material selected from the group consisting of glass, silicon, fused silica, plastic, ceramic, and metal.

25. A method for mixing a film of fluid, comprising:  
providing a first substrate and a substantially parallel second substrate having inner surfaces that define a closed chamber therebetween, said chamber adapted to retain a quantity of fluid so that the fluid is in contact with both inner surfaces;

introducing a fluid containing a plurality of components into the closed chamber so as to provide a film of fluid therein; and

nucleating a bubble within the film of fluid, whereby, as the bubble is nucleated and dispelled, the fluid is displaced resulting in mixing.

26. The method of claim 25 further comprising moving a bubble in the fluid.

27. The method of claim 25 wherein said step of nucleating bubbles also comprises moving a bubble in the fluid.

28. The method of claim 25 wherein said step of nucleating a bubble comprises heating using a plurality of discrete heat sources adjacent one of said inner surfaces.

29. The method of claim 25 wherein the means for nucleating a bubble comprises heating using a plurality of discrete heat sources adjacent both of said inner surfaces.

30. The method of claim 28 wherein the discrete heat sources comprise resistors arranged in a predetermined pattern.

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31. The method of claim 25 wherein one of said inner surfaces is functionalized with reactive moieties.

32. The method of claim 25 wherein each of said inner surfaces is functionalized with reactive moieties.

33. The method of claim 31 wherein the reactive moieties comprise monomeric species covalently bound to the inner surface, each of the monomeric species having at least one reactive site.

34. The method of claim 33 wherein the monomeric species are nucleotides.

35. The method of claim 35 wherein the monomeric species are amino acids.

36. The method of claim 31 wherein the reactive moieties comprise reactive sites of monomeric species present at the terminus of a surface-bound polymer.

37. The method of claim 36 wherein the surface-bound polymer comprises a polynucleotide.

38. The method of claim 36 wherein the surface-bound polymer comprises a polynucleotide.

39. The method of claim 36 wherein the surface-bound polymer comprises a polypeptide.

40. The method of claim 25, further including introducing fluid into the closed chamber to provide a film of fluid therein.

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4) The method of claim 25, further including defining the thickness of the film by enclosing the fluid between said surfaces and ensuring that the film is retained in the closed chamber.

Please add the following new claims:

6  
42. (NEW) The apparatus of claim 4 wherein said means for nucleating bubbles also comprises means for moving a bubble in the fluid.

12  
43. (NEW) The apparatus of claim 4 wherein said means for nucleating bubbles also comprises means for moving a bubble in the fluid.

A3  
13  
44. (NEW) The apparatus of claim 4 wherein the reactive moieties comprise polynucleotide, polyribonucleotide, or polypeptide.

#### Remarks

The Examiner is thanked for the Office Action mailed 11/24/99, and the allowance of claims 25-41 and the indication of allowability of claims 3 and 20 (if rewritten in independent form). The Examiner's rejections of the other claims are discussed in sequence below. New claims 42, 43 use the limitation of claim 3, while new claim 44 uses limitations in claims 37-39.

#### 35 USC 112

The Examiner first rejected claim 20 under 35 U.S.C. 112, second paragraph, on the basis that the phrase "the discrete heat sources" lacked antecedent basis. The above amendments to claims 16 and 18 correct this, such that this rejection should now be withdrawn.

#### 35 USC 102

The Examiner next rejected claims 1, 4, 5, 15, 21, 23 and 24 under 35 U.S.C. 102(b) as being anticipated by Oberhardt. However, as the Examiner is aware, every

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element must be found in the cited reference in order to establish a case of anticipation. In the present case, one distinction between claim 1 and Oberhardt's apparatus, is that claim 1 requires "means for nucleating bubbles in the fluid comprising discrete heat sources for creating individual bubbles at selected locations within the apparatus". Thus, claim 1 (and the remainder of these rejected claims which are dependent upon claim 1) recites heat sources (i.e. more than one heat source). The Examiner references only the single heat source 238 of Oberhardt. For this reason alone, this rejection should be withdrawn.

In addition to the above, claim 1 (and the remainder of the rejected claims) requires "means for nucleating bubbles in the fluid comprising discrete heat sources for creating individual bubbles at selected locations". The Examiner states that although Oberhardt does not expressly teach that the heat source is "for nucleating bubbles", it inherently fulfills the foregoing limitation. However, this is not necessarily true. In particular, as pointed out in column 25, lines 20-53 the apparatus of FIG. 35 is simply for measuring the heat capacity of a liquid by measuring temperature change resulting from a known amount of heat being applied through heater 238 (see particularly, col. 25, lines 46-52). It is not disclosed in this that heater 238 can provide sufficient heat to the liquid to cause bubble formation without heater burnout. Various factors determine whether this is possible, including the capacity of heater 238 and the heat conductance of other components of the apparatus. While *\*.* presumably one could increase the voltage to heater 238 it is not clear that heater 238 is of a construction which would nucleate bubble formation before burning out (or causing some other problem). While it is possible that heater 238 might be of such a construction, this does not rise to the level of inherency. As stated by the Federal Circuit *In re Robertson* 49 USPQ2d 1949 (Fed.Cir., 1999) @ p.1950-1951:

"If the prior art reference does not expressly set forth a particular element of the claim, that reference still may anticipate if that element is "inherent" in its disclosure. To establish inherency, the extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir. 1991). "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *Id.* at

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1269, 20 U.S.P.Q.2d at 1749 (quoting *In re Oelrich*, 666 F.2d 578, 581, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981))."

Thus, the fact that the heater 238 may be of sufficient heating capacity to nucleate bubbles, does not establish anticipation. For this additional reason, the anticipation rejection should be withdrawn.

### 35 USC 103

The Examiner next rejected claims 2, 6-14, 16, 18 and 19 under 35 U.S.C. 103(a) as being unpatentable over Oberhardt. First, as pointed out above, Oberhardt's heater 238 is for providing sufficient heat to a liquid such that its heat capacity can be measured, and the reference does not disclose that heater 238 should be of a sufficient capacity to nucleate bubbles. Furthermore, there is no suggestion or motivation in Oberhardt or other cited prior art for one to ensure that heater 238 does have sufficient heat capacity for nucleation. In fact, the suggestion is to the contrary - if only heat capacity of a liquid is to be measured, heater 238 should probably be of a relatively low capacity to use less materials and keep size small. While again heater 238 might be modified to ensure that it has sufficient capacity to nucleate bubble formation, as pointed out by the Federal Circuit in *In re Fritch* 23 USPQ2d 1780 (Fed.Cir. 1992) @ 1783-1784:

"The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification" (citation omitted)"

For the above reason alone, the rejection based on obviousness over Oberhardt should be withdrawn.

In addition to the above, all of the claims rejected for obviousness are directly or indirectly dependent upon claim 1. As pointed out above, these claims all require heat sources (i.e. more than one heat source). With respect to this feature, the Examiner states that "it is deemed obvious to use more than one heater for increase temperature change of the fluid. It is well settled to increase parts for a multiplied effect". However, as the Examiner is aware, the prior art must suggest the desirability of making the modification (see, for example, *In re Fritch* above), not the Examiner.

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Oberhardt in FIG. 35 is dealing only with measuring the heat capacity of a liquid. There is no reason to obtain a "multiplied effect" as the Examiner suggests, since further heating is not required. In fact, if anything, Oberhardt would suggest to one of ordinary skill to have only one heater 238 as shown, since this will be sufficient to measure heat capacity and it is generally undesirable to increase the number of parts without reason.

For the foregoing additional reason, the rejection based on obviousness over Oberhardt should be withdrawn.

In further addition to the above, even if the Examiner has established a *prima facie* case of obviousness, such can be rebutted by a showing of unexpected advantage. In the present case even if, as the Examiner alleges, it would have been obvious to modify Oberhardt in a manner which provides multiple heaters each of sufficient capacity to nucleate bubble formation (which is disputed above), the ability to thereby be able to move bubbles around and cause mixing of fluid as taught in the present application is not suggested by Oberhardt and is unexpected. Thus, for this further additional reason, the obviousness rejection based on Oberhardt should be withdrawn.

In summary, for any one of the above reasons, the obviousness rejection based on Oberhardt should be withdrawn. However, particularly when considered together it is submitted that it is clear that the rejection should be withdrawn.

#### Conclusion

In view of the above amendments and discussion, claims 1, 2, 4-19 and 21-24,




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and new claims 42-44 should also be allowable in addition to allowed claims 25-41 and allowable claims 3 and 20. If the Examiner is of the view that there are any outstanding issues that might be resolved by means of a telephone conference, he is invited to call Gordon Stewart at (650)236-2386.

Respectfully submitted

  
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February 23, 2000  
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gmw10971849-1 First Response